

SEQUENCE LISTING

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Lazdunski, Michel

<120> FAMILY OF MAMMALIAN POTASSIUM CHANNELS, THEIR CLONING
AND THEIR USE, ESPECIALLY FOR THE SCREENING OF DRUGS

<130> 1201-CIP-DIV-2-00

<141> 2001-08-24

<150> 09/144,914

<151> 1998-09-01

<150> 08/749,816

<151> 1996-11-15

<150> 60/095,234

<151> 1998-08-04

<150> FR 96/01565

<151> 1996-02-08

<160> 24

<170> PatentIn Ver. 2.0

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<213> Homo sapiens

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<222> (183)..(1190)

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<223> TWIK-1

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cgcgctccgg ccggtctgcg gcgttggcct tggctttggc tttggcgcg cggttgaga 180

ag atg ctg cag tcc ctg gcc ggc agc tcg tgc gtg cgc ctg gtg gag 227
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Arg His Arg Ser Ala Trp Cys Phe Gly Phe Leu Val Leu Gly Tyr Leu
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ctc tac ctg gtc ttc ggc gca gtg gtc ttc tcc tcg gtg gag ctg ccc 323
Leu Tyr Leu Val Phe Gly Ala Val Val Phe Ser Ser Val Glu Leu Pro
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tat gag gac ctg ctg cgc cag gag ctg cgc aag ctg aag cga cgc ttc 371
Tyr Glu Asp Leu Leu Arg Gln Glu Leu Arg Lys Leu Lys Arg Arg Phe
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Leu Glu Glu His Glu Cys Leu Ser Glu Gln Gln Leu Glu Gln Phe Leu
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Gly Arg Val Leu Glu Ala Ser Asn Tyr Gly Val Ser Val Leu Ser Asn
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gcc tgc ggc aac tgg aac tgg gac ttc acc tcc gcg ctc ttc ttc gcc 515
Ala Ser Gly Asn Trp Asn Trp Asp Phe Thr Ser Ala Leu Phe Phe Ala
100 105 110

agc acc gtg ctc tcc acc aca ggt tat ggc cac acc gtg ccc ttg tca 563
Ser Thr Val Leu Ser Thr Thr Gly Tyr Gly His Thr Val Pro Leu Ser
115 120 125

gat gga ggt aag gcc ttc tgc atc atc tac tcc gtc att ggc att ccc 611
Asp Gly Gly Lys Ala Phe Cys Ile Ile Tyr Ser Val Ile Gly Ile Pro
130 135 140

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Phe Thr Leu Leu Phe Leu Thr Ala Val Val Gln Arg Ile Thr Val His
145 150 155

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Val Thr Arg Arg Pro Val Leu Tyr Phe His Ile Arg Trp Gly Phe Ser
160 165 170 175

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Lys Gln Val Val Ala Ile Val His Ala Val Leu Leu Gly Phe Val Thr
180 185 190

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Val Ser Cys Phe Phe Phe Ile Pro Ala Ala Val Phe Ser Val Leu Glu
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Asp Asp Trp Asn Phe Leu Glu Ser Phe Tyr Phe Cys Phe Ile Ser Leu
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agc acc att ggc ctg ggg gat tat gtg cct ggg gaa ggc tac aat caa 899
Ser Thr Ile Gly Leu Gly Asp Tyr Val Pro Gly Glu Gly Tyr Asn Gln
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aaa ttc aga gag ctc tat aag att ggg atc acg tgt tac ctg cta ctt 947
Lys Phe Arg Glu Leu Tyr Lys Ile Gly Ile Thr Cys Tyr Leu Leu Leu
240 245 250 255

ggc ctt att gcc atg ttg gta gtt ctg gaa acc ttc tgt gaa ctc cat 995
Gly Leu Ile Ala Met Leu Val Val Leu Glu Thr Phe Cys Glu Leu His
260 265 270

gag ctg aaa aaa ttc aga aaa atg ttc tat gtg aag aag gac aag gac 1043
Glu Leu Lys Lys Phe Arg Lys Met Phe Tyr Val Lys Lys Asp Lys Asp
275 280 285

gag gat cag gtg cac atc ata gag cat gac caa ctg tcc ttc tcc tcg 1091

00030403 0002401

Glu Asp Gln Val His Ile Ile Glu His Asp Gln Leu Ser Phe Ser Ser
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atc aca gac cag gca gct ggc atg aaa gag gac cag aag caa aat gag 1139
 Ile Thr Asp Gln Ala Ala Gly Met Lys Glu Asp Gln Lys Gln Asn Glu
 305 310 315

cct ttt gtg gcc acc cag tca tct gcc tgc gtg gat ggc cct gca aac 1187
 Pro Phe Val Ala Thr Gln Ser Ser Ala Cys Val Asp Gly Pro Ala Asn
 320 325 330 335

cat tgagcgtagg atttggtgca ttatgctaga gcaccagggg caggggtgcaa 1240
 His

ggaagagggt taagtatggt catttttatc agaatgcaaa agcgaaaatt atgtcacttt 1300

aagaaatagc tactgtttgc aatgtcttat taaaaaacia caaaaaaaga cacatggaac 1360

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<213> Homo sapiens

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 35 40 45

Glu Asp Leu Leu Arg Gln Glu Leu Arg Lys Leu Lys Arg Arg Phe Leu
 50 55 60

Glu Glu His Glu Cys Leu Ser Glu Gln Gln Leu Glu Gln Phe Leu Gly
 65 70 75 80

Arg Val Leu Glu Ala Ser Asn Tyr Gly Val Ser Val Leu Ser Asn Ala
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 Ser Gly Asn Trp Asn Trp Asp Phe Thr Ser Ala Leu Phe Phe Ala Ser
 100 105 110
 Thr Val Leu Ser Thr Thr Gly Tyr Gly His Thr Val Pro Leu Ser Asp
 115 120 125
 Gly Gly Lys Ala Phe Cys Ile Ile Tyr Ser Val Ile Gly Ile Pro Phe
 130 135 140
 Thr Leu Leu Phe Leu Thr Ala Val Val Gln Arg Ile Thr Val His Val
 145 150 155 160
 Thr Arg Arg Pro Val Leu Tyr Phe His Ile Arg Trp Gly Phe Ser Lys
 165 170 175
 Gln Val Val Ala Ile Val His Ala Val Leu Leu Gly Phe Val Thr Val
 180 185 190
 Ser Cys Phe Phe Phe Ile Pro Ala Ala Val Phe Ser Val Leu Glu Asp
 195 200 205
 Asp Trp Asn Phe Leu Glu Ser Phe Tyr Phe Cys Phe Ile Ser Leu Ser
 210 215 220
 Thr Ile Gly Leu Gly Asp Tyr Val Pro Gly Glu Gly Tyr Asn Gln Lys
 225 230 235 240
 Phe Arg Glu Leu Tyr Lys Ile Gly Ile Thr Cys Tyr Leu Leu Leu Gly
 245 250 255
 Leu Ile Ala Met Leu Val Val Leu Glu Thr Phe Cys Glu Leu His Glu
 260 265 270
 Leu Lys Lys Phe Arg Lys Met Phe Tyr Val Lys Lys Asp Lys Asp Glu
 275 280 285
 Asp Gln Val His Ile Ile Glu His Asp Gln Leu Ser Phe Ser Ser Ile
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 <222> (126)..(1307)

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ggacg atg aag cgg cag aac gtg cgc acg ctg gcg ctc atc gtg tgc acc 170

Met Lys Arg Gln Asn Val Arg Thr Leu Ala Leu Ile Val Cys Thr
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ttc acc tac ctg ctg gtg ggc gcc gcg gtc ttc gac gcg ctg gag tgc 218
Phe Thr Tyr Leu Leu Val Gly Ala Ala Val Phe Asp Ala Leu Glu Ser
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gag ccc gag ctg atc gag cgg cag cgg ctg gag ctg cgg cag cag gag 266
Glu Pro Glu Leu Ile Glu Arg Gln Arg Leu Glu Leu Arg Gln Gln Glu
35 40 45

ctg cgg gcg cgc tac aac ctc agc cag ggc ggc tac gag gag ctg gag 314
Leu Arg Ala Arg Tyr Asn Leu Ser Gln Gly Gly Tyr Glu Glu Leu Glu
50 55 60

cgc gtc gtg ctg cgc ctc aag ccg cac aag gcc ggc gtg cag tgg cgc 362
Arg Val Val Leu Arg Leu Lys Pro His Lys Ala Gly Val Gln Trp Arg
65 70 75

ttc gcc ggc tcc ttc tac ttc gcc atc acc gtc atc acc acc atc ggc 410
Phe Ala Gly Ser Phe Tyr Phe Ala Ile Thr Val Ile Thr Thr Ile Gly
80 85 90 95

tac ggg cac gcg gca ccc agc acg gat ggc ggc aag gtg ttc tgc atg 458
Tyr Gly His Ala Ala Pro Ser Thr Asp Gly Gly Lys Val Phe Cys Met
100 105 110

ttc tac gcg ctg ctg ggc atc ccg ctc acg ctc gtc atg ttc cag agc 506
Phe Tyr Ala Leu Leu Gly Ile Pro Leu Thr Leu Val Met Phe Gln Ser
115 120 125

ctg gcc gag cgc atc aac acc ttg gtg agg tac ctg ctg cac cgc gcc 554
Leu Gly Glu Arg Ile Asn Thr Leu Val Arg Tyr Leu Leu His Arg Ala
130 135 140

aag aag ggg ctg ggc atg cgg cgc gcc gac gtg tcc atg gcc aac atg 602
Lys Lys Gly Leu Gly Met Arg Arg Ala Asp Val Ser Met Ala Asn Met
145 150 155

gtg ctc atc gcc ttc ttc tgc tgc atc agc acg ctg tgc atc gcc gcc 650
Val Leu Ile Gly Phe Phe Ser Cys Ile Ser Thr Leu Cys Ile Gly Ala
160 165 170 175

gcc gcc ttc tcc cac tac gag cac tgg acc ttc ttc cag gcc tac tac 698
Ala Ala Phe Ser His Tyr Glu His Trp Thr Phe Phe Gln Ala Tyr Tyr
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tac tgc ttc atc acc ctc acc acc atc ggc ttc ggc gac tac gtg gcg 746
Tyr Cys Phe Ile Thr Leu Thr Thr Ile Gly Phe Gly Asp Tyr Val Ala
195 200 205

ctg cag aag gac cag gcc ctg cag acg cag ccg cag tac gtg gcc ttc 794
Leu Gln Lys Asp Gln Ala Leu Gln Thr Gln Pro Gln Tyr Val Ala Phe
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 Ser Phe Val Tyr Ile Leu Thr Gly Leu Thr Val Ile Gly Ala Phe Leu
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aac ctc gtg gtg ctg cgc ttc atg acc atg aac gcc gag gac gag aag 890
 Asn Leu Val Val Leu Arg Phe Met Thr Met Asn Ala Glu Asp Glu Lys
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cgc gac gcc gag cac cgc gcg ctg ctc acg cgc aac ggg cag gcg ggc 938
 Arg Asp Ala Glu His Arg Ala Leu Leu Thr Arg Asn Gly Gln Ala Gly
 260 265 270

ggc ggc gga ggg ggt ggc agc gcg cac act acg gac acc gcc tca tcc 986
 Gly Gly Gly Gly Gly Gly Ser Ala His Thr Thr Asp Thr Ala Ser Ser
 275 280 285

acg gcg gca gcg ggc ggc ggc ggc ttc cgc aac gtc tac gcg gag gtg 1034
 Thr Ala Ala Ala Gly Gly Gly Gly Phe Arg Asn Val Tyr Ala Glu Val
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ctg cac ttc cag tcc atg tgc tgc tgc ctg tgg tac aag agc cgc gag 1082
 Leu His Phe Gln Ser Met Cys Ser Cys Leu Trp Tyr Lys Ser Arg Glu
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 Lys Leu Gln Tyr Ser Ile Pro Met Ile Ile Pro Arg Asp Leu Ser Thr
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tcc gac acg tgc gtg gag cag agc cac tgc tgc ccg gga ggg ggc ggc 1178
 Ser Asp Thr Cys Val Glu Gln Ser His Ser Ser Pro Gly Gly Gly Gly
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cgc tac agc gac acg ccc tgc cga cgc tgc ctg tgc agc ggg gcg cca 1226
 Arg Tyr Ser Asp Thr Pro Ser Arg Arg Cys Leu Cys Ser Gly Ala Pro
 355 360 365

cgc tcc gcc atc agc tgc gtg tcc acg ggt ctg cac agc ctg tcc acc 1274
 Arg Ser Ala Ile Ser Ser Val Ser Thr Gly Leu His Ser Leu Ser Thr
 370 375 380

ttc cgc ggc ctc atg aag cgc agg agc tcc gtg tgactgcccc gagggacctg 1327
 Phe Arg Gly Leu Met Lys Arg Arg Ser Ser Val
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 <213> Homo sapiens

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 Pro Glu Leu Ile Glu Arg Gln Arg Leu Glu Leu Arg Gln Gln Glu Leu
 35 40 45
 Arg Ala Arg Tyr Asn Leu Ser Gln Gly Gly Tyr Glu Glu Leu Glu Arg
 50 55 60
 Val Val Leu Arg Leu Lys Pro His Lys Ala Gly Val Gln Trp Arg Phe
 65 70 75 80
 Ala Gly Ser Phe Tyr Phe Ala Ile Thr Val Ile Thr Thr Ile Gly Tyr
 85 90 95
 Gly His Ala Ala Pro Ser Thr Asp Gly Gly Lys Val Phe Cys Met Phe
 100 105 110
 Tyr Ala Leu Leu Gly Ile Pro Leu Thr Leu Val Met Phe Gln Ser Leu
 115 120 125
 Gly Glu Arg Ile Asn Thr Leu Val Arg Tyr Leu Leu His Arg Ala Lys
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 Lys Gly Leu Gly Met Arg Arg Ala Asp Val Ser Met Ala Asn Met Val

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35 40 45

Tyr Asn Leu Ser Glu Gly Gly Tyr Glu Glu Leu Glu Arg Val Val Leu
50 55 60

Arg Leu Lys Pro His Lys Ala Gly Val Gln Trp Arg Phe Ala Gly Ser
65 70 75 80

Phe Tyr Phe Ala Ile Thr Val Ile Thr Thr Ile Gly Tyr Gly His Ala
85 90 95

Ala Pro Ser Thr Asp Gly Gly Lys Val Phe Cys Met Phe Tyr Ala Leu
100 105 110

Leu Gly Ile Pro Leu Thr Leu Ile Met Phe Gln Ser Leu Gly Glu Arg
115 120 125

Ile Asn Thr Phe Val Arg Tyr Leu Leu His Arg Ala Lys Arg Gly Leu
130 135 140

Gly Met Arg His Ala Glu Val Ser Met Ala Asn Met Val Leu Ile Gly
145 150 155 160

Phe Val Ser Cys Ile Ser Thr Leu Cys Ile Gly Ala Ala Ala Phe Ser
165 170 175

Tyr Tyr Glu Arg Trp Thr Phe Phe Gln Ala Tyr Tyr Tyr Cys Phe Ile
180 185 190

Thr Leu Thr Thr Ile Gly Phe Gly Asp Tyr Val Ala Leu Gln Lys Asp
195 200 205

Gln Ala Leu Gln Thr Gln Pro Gln Tyr Val Ala Phe Ser Phe Val Tyr
210 215 220

Ile Leu Thr Gly Leu Thr Val Ile Gly Ala Phe Leu Asn Leu Val Val
225 230 235 240

Leu Arg Phe Met Thr Met Asn Ala Glu Asp Glu Lys Arg Asp Ala Glu
245 250 255

His Arg Ala Leu Leu Thr His Asn Gly Gln Ala Val Gly Leu Gly Gly
260 265 270

Leu Ser Cys Leu Ser Gly Ser Leu Gly Asp Val Arg Pro Arg Asp Pro
275 280 285

Val Thr Cys Ala Ala Ala Ala Gly Gly Val Gly Val Gly Val Gly Gly
290 295 300

Ser Gly Phe Arg Asn Val Tyr Ala Glu Val Leu His Phe Gln Ser Met
305 310 315 320

Cys Ser Cys Leu Trp Tyr Lys Ser Arg Glu Lys Leu Gln Tyr Ser Ile
325 330 335

Pro Met Ile Ile Pro Arg Asp Leu Ser Thr Ser Asp Thr Cys Val Glu
340 345 350

09039483 082401

His Ser His Ser Ser Pro Gly Gly Gly Gly Arg Tyr Ser Asp Thr Pro
 355 360 365

Ser His Pro Cys Leu Cys Ser Gly Thr Gln Arg Ser Ala Ile Ser Ser
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Val Ser Thr Gly Leu His Ser Leu Ala Ala Phe Arg Gly Leu Met Lys
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Arg Arg Ser Ser Val
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 <212> PRT
 <213> Unknown

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 35 40 45

Phe Asn Leu Ile Gly Ala Gly Ile Phe Tyr Leu Ala Glu Thr Gln Asn
 50 55 60

Ser Ser Glu Ser Leu Asn Glu Asn Ser Glu Val Ser Lys Cys Leu His
 65 70 75 80

Asn Leu Pro Ile Gly Gly Lys Ile Thr Ala Glu Met Lys Ser Lys Leu
 85 90 95

Gly Lys Cys Leu Thr Lys Ser Ser Arg Ile Asp Gly Phe Gly Lys Ala
 100 105 110

Ile Phe Phe Ser Trp Thr Leu Tyr Ser Thr Val Gly Tyr Gly Ser Leu
 115 120 125

Tyr Pro His Ser Thr Leu Gly Arg Tyr Leu Thr Ile Phe Tyr Ser Leu
 130 135 140

Leu Met Ile Pro Val Phe Ile Ala Phe Lys Phe Glu Phe Gly Thr Phe
 145 150 155 160

Leu Ala His Phe Leu Val Val Val Ser Asn Arg Thr Arg Leu Ala Val
 165 170 175

Lys Lys Ala Tyr Tyr Lys Leu Ser Gln Asn Pro Glu Asn Ala Glu Thr
 180 185 190

Pro Ser Asn Ser Leu Gln His Asp Tyr Leu Ile Phe Leu Ser Ser Leu
 195 200 205

Lys Pro Arg Leu Ser Phe Ser Ser Lys Pro Thr Val Leu Ala Ser Arg
20 25 30

Val Glu Ser Asp Ser Ala Ile Asn Val Met Lys Trp Lys Thr Val Ser
35 40 45

Thr Ile Phe Leu Val Val Val Leu Tyr Leu Ile Ile Gly Ala Ala Val
50 55 60

Phe Lys Ala Leu Glu Gln Pro Gln Glu Ile Ser Gln Arg Thr Thr Ile
65 70 75 80

Val Ile Gln Lys Gln Thr Phe Ile Ala Gln His Ala Cys Val Asn Ser
85 90 95

Thr Glu Leu Asp Glu Leu Ile Gln Gln Ile Val Ala Ala Ile Asn Ala
100 105 110

Gly Ile Ile Pro Leu Gly Asn Ser Ser Asn Gln Val Ser His Trp Asp
115 120 125

Leu Gly Ser Ser Phe Phe Phe Ala Gly Thr Val Ile Thr Thr Ile Gly
130 135 140

Phe Gly Asn Ile Ser Pro Arg Thr Glu Gly Gly Lys Ile Phe Cys Ile
145 150 155 160

Ile Tyr Ala Leu Leu Gly Ile Pro Leu Glu Gly Phe Leu Leu Ala Gly
165 170 175

Val Gly Asp Gln Leu Gly Thr Ile Phe Gly Lys Gly Ile Ala Lys Val
180 185 190

Glu Asp Thr Phe Ile Lys Trp Asn Val Ser Gln Thr Lys Ile Arg Ile
195 200 205

Ile Ser Thr Ile Ile Phe Ile Leu Phe Gly Cys Val Leu Phe Val Ala
210 215 220

Leu Pro Ala Val Ile Phe Lys His Ile Glu Gly Trp Ser Ala Leu Asp
225 230 235 240

Ala Ile Tyr Phe Val Val Ile Thr Leu Thr Thr Ile Gly Phe Gly Asp
245 250 255

Tyr Val Ala Gly Gly Ser Asp Ile Glu Tyr Leu Asp Phe Tyr Lys Pro
260 265 270

Val Val Trp Phe Trp Ile Leu Val Gly Leu Ala Tyr Phe Ala Ala Val
275 280 285

Leu Ser Met Ile Gly Asp Trp Leu Arg Val Ile Ser Lys Lys Thr Lys
290 295 300

Glu Glu Val Gly Glu Phe Arg Ala His Ala Ala Glu Trp Thr Ala Asn
305 310 315 320

Val Thr Ala Glu Phe Lys Glu Thr Arg Arg Arg Leu Ser Val Glu Ile
325 330 335

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Cys Leu
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<213> Homo sapiens

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<223> TWIK-1 P1

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Tyr Gly His Thr Val Pro Leu Ser Asp Gly Gly
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<212> PRT
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<220>
<223> TWIK-1 P2

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Leu Gly Asp Tyr Val Pro Gly Glu Gly Tyr Asn
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<213> Unknown

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representative K⁺ channel sequence

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representative K+ channel sequence

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<223> TOK-1 P1

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1 5 10 15
Leu Gly Asp Ile Leu Pro Lys Ser Val Gly Ala
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Tyr Gly Asp Val Tyr Cys Glu Thr Val Leu Gly
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Tyr Gly Asp Met Thr Pro Val Gly Phe Trp Gly
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<212> PRT
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representative K+ channel sequence

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representative K+ channel sequence

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<223> Shal
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representative K+ channel sequence

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representative K+ channel sequence

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Tyr Gly Tyr Arg Tyr Ile Thr Asp Lys Cys Pro
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